CLAIMS

We claim:

1. A structurally biased integrin I domain protein comprising an amino acid sequence that is less than about 98% identical to human integrin I domain protein wherein the alterations to the protein occur in at least two noncontiguous regions wherein said integrin I domain protein is artificially biased to exist in an "open" conformation.

2. A full length integrin comprising the domain of claim 1.

3. A non-naturally occurring integrin I domain protein comprising at least 3 amino acid substitutions as compared to human integrin I domain protein, wherein at least 2 of said substitutions are selected from the amino acid residues at positions selected from positions 139, 153,156, 157, 160, 199, 215, 219, 223, 238, 239, 240, 259, 269, 271, 287, 299, 308.

4. The non-naturally occurring integrin I domain protein according to claim 3 comprising substitutions at positions 156, 160, 199, 215, 238, 239, 240, 259, 269, 271, 287, 299, 308.

5. The non-naturally occurring integrin I domain protein according to claim 3 comprising substitutions at positions 156, 199, 215, 238, 239, 240, 259, 287, 299.

6. The non-naturally occurring integrin I domain protein according to claim 3 comprising substitutions at positions 139, 153, 157, 199, 238, 239, 287, 299.

7. The non-naturally occurring integrin I domain protein according to claim 3 comprising substitutions at positions 215, 219, 223, 238.

8. A recombinant nucleic acid encoding the non-naturally occurring integrin I domain protein of claim 1, 2 or 3.

9. An expression vector comprising the recombinant nucleic acid of claim 8.

10. A host cell comprising the recombinant nucleic acid of claim 8.

11. A host cell comprising the expression vector of claim 8.

12. A method of producing a non-naturally occurring integrin I domain protein comprising culturing the host cell of claim 10 under conditions suitable for expression of said nucleic acid.

13. The method according to claim 12 further comprising recovering said integrin I domain protein.

14. A pharmaceutical composition comprising an integrin I domain protein according to claim 1, 2, or 3 and a pharmaceutical carrier.

15. A method for screening for modulators that bind to the open conformation of the integrin protein of claim 1, 2, or 3 comprising the steps of:

(A) combining a candidate agent with an integrin that is artificially biased to exist in the open conformation, where the artificial bias is a result of noncontiguous alterations of the protein, these alterations resulting in a protein that is less than 98% identical to the wild-type protein.

(B) determining the binding of the agent to the integrin (or I domain);

16. The method in claim 15 where the screen is for modulators that will also bind to the closed conformation.

17. A method for making an antibody which binds to the protein in claim 1, 2, or 3 using the protein from claim 1, 2, or 3.

18. The method in claim 17 wherein said Ab is monoclonal.

19. The method in claim 17 wherein said Ab binds to the open conformation but not the closed conformation.

20. A method as in claim 17 wherein said Ab binds to the structurally biased closed protein structure but not the open conformation.

21. A method executed by a computer under the control of a program, said computer including a memory for storing said program and said method comprising the steps of:

(A) receiving an integrin protein backbone structure with variable residue positions;

(B) establishing a group of potential rotamers for each group of said variable residue positions

(C) analyzing the interaction of each of said rotamers with all or part of the remainder of said protein to generate a set of protein sequences optimized for at least one scoring function.

22. A method for treating an integrin I domain responsive condition comprising administering an integrin I domain protein according to claim 1, 2, or 3 to a patient.

23. The method according to claim 22, wherein said condition is an autoimmune disease.

24. The method according to claim 22, wherein said condition is an inflammatory disease.

25. The method according to claim 22, wherein said condition is a transplant rejection.

26. The method according to claim 22, wherein said condition is an ischemia/reperfusion as in hypovolemic shock, myocardial infarct and cerebral shock

27. The method according to claim 22, wherein said condition is a viral infection.

28. The method according to claim 22 wherein said condition is a cancer.

29. A composition comprising an integrin that is artificially biased to exist in the open conformation, where the artificial bias is a result of noncontiguous alterations of the protein, these alterations resulting in a protein that is less than 98% identical to the wild-type protein, crystalized with ligand.

30. A composition comprising an integrin that is artificially biased to exist in the closed conformation, where the artificial bias is a result of noncontiguous alterations of the protein, these alterations resulting in a protein that is less than 98% identical to the wild-type protein, crystalized with ligand.